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Walking Capacity Is Positively Related with Heart Rate Variability in Symptomatic Peripheral Artery Disease

A.H.R.A. Lima [a,*], A.H.G. Soares [b], G.G. Cucato [c], A.S. Leicht [d], F.G.M. Franco [c], N. Wolosker [c], R.M. Ritti-Dias [c]

[a] School of Physical Education and Sport, University of São Paulo, São Paulo, Brazil
[b] School of Physical Education, University of Pernambuco, Pernambuco, Brazil
[c] Albert Einstein Israelite Hospital, São Paulo, Brazil
[d] Sport and Exercise Science, James Cook University, Townsville, Queensland, Australia

WHAT THIS PAPER ADDS
Enhancement of walking capacity may be a simple means for patients with symptomatic peripheral artery disease to augment heart rate variability (HRV) and reduce cardiovascular risk. The current results reinforce the need to implement clinical strategies to increase physical activity and walking capacity in these patients.

Objectives: The aim was to investigate the association between walking capacity and HRV in patients with symptomatic peripheral artery disease (PAD).
Methods: This was a cross sectional study. Ninety-five patients were recruited. Patients undertook a supine position for 20 minutes, with the final 10 minutes used to examine for resting HRV. Time domain, frequency domain, and non-linear indices were evaluated. A maximal treadmill test (Gardner protocol) was performed to assess maximal walking distance (MWD) and claudication distance (CD) in groups of PAD patients based upon their walking abilities (low, moderate, high). Differences between PAD patient groups were examined using non-parametric analyses, and Spearman rank correlations identified the relationship between MWD and CD, and HRV parameters.
Results: Symptomatic PAD patients with high MWD exhibited significantly greater HRV than patients with low MWD. Furthermore, MWD was positively associated with time domain and non-linear indices of HRV (all $p < .05$). However, no statistically significant correlations were observed between CD and HRV parameters or between PAD groups.
Conclusion: A greater walking capacity is associated with better HRV in symptomatic PAD patients.

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INTRODUCTION

Peripheral artery disease (PAD) affects more than 200 million people worldwide[1] and is characterized by the narrowing of the peripheral arteries of the body, especially in the lower limbs.[2] The symptoms of PAD are characterized by a sensation of pain, cramping or burning that occurs in the affected limb during physical activity.[3,4] This symptomology limits walking capacity,[5] leading to a reduction in patient quality of life.[6]

Besides walking impairment, patients with symptomatic PAD present with several risk factors and comorbidities, including hypertension, obesity, diabetes, smoking, and dyslipidemia.[7,8] These conditions are known to promote an imbalance between parasympathetic and sympathetic modulations of the heart,[9,10] as reflected by reduced heart rate variability (HRV). It is well documented that low HRV is a strong and independent predictor of cardiovascular disease incidence and mortality for both healthy people and those with diagnosed cardiovascular disease.[11,12] Interestingly, high levels of physical activity and improvements in aerobic fitness have been demonstrated to reduce cardiovascular risk and improvement of cardiac autonomic function in healthy[10,13] and clinical populations.[14]

In symptomatic PAD patients, the imbalance in cardiac autonomic modulation was previously described by Goernig et al.,[15] with patients presenting low HRV compared with patients with cardiovascular disease but without PAD. More recently, Chen et al.[16] reported that the HRV response (i.e. lack of change) during hemodialysis was impaired in

* Corresponding author. School of Physical Education and Sport, University of São Paulo, Av. Professor Melo Moraes, 65, 05508-030 São Paulo, SP, Brazil.
E-mail address: aluisiolima@live.com (A.H.R.A. Lima).
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patients with PAD compared with individuals without PAD. However, neither of these studies considered walking capacity or fitness level as a contributing factor to HRV control in PAD patients. Given that PAD patients with higher walking capacity exhibit better clinical status,[17,18] it is possible that patients with a greater walking capacity will present greater HRV than patients with lower walking capacity.

Previously, we reported that HRV increased similarly over 12 months for two groups of symptomatic PAD patients, despite significant differences in walking capacity change (183 vs. 57%; $p = .03$).[19] This previous study examined a small cohort of patients, with larger studies needed to examine further the relationship between walking capacity and HRV in PAD patients. Therefore, the aim of the present study was to investigate, in a larger study, the association between walking capacity and HRV in patients with symptomatic PAD. Significant relationships between walking capacity and HRV may provide further support for targeted interventions to enhance cardiac autonomic function, reduce cardiovascular risk, and improve long-term prognosis for symptomatic PAD patients.

MATERIALS AND METHODS

Participants and study overview

Ninety-five patients with symptomatic PAD were recruited through public hospitals and private vascular clinics in Pernambuco and São Paulo, Brazil. Patients were included if they met the following criteria: (a) ankle/brachial index (ABI) $\leq$ 0.90 in at least one lower limb[20]; (b) non-compressible vessels; (c) age $>$ 50 years old; (d) no history of lower limb bypass surgery or angioplasty within the past year; (e) no previous lower limb amputation, ulcers, or rest pain; and (f) not performing any regular exercise within the last 6 months (i.e. three times per week of 30 minutes' duration). Furthermore, patients were excluded if they had asymptomatic PAD. Patients underwent an initial screening visit to familiarize themselves with the study procedures. On a subsequent day, patients performed a graded treadmill walking test to determine their maximal walking capacity followed by a resting HRV examination on a different day, at least 48—72 hours after the walking test. This study was approved by the Human Research Ethics Committees of the University of Pernambuco (process 0134/09). Patients were informed about the risks and benefits of the study and provided informed written consent prior to participation. Based on a study of HRV in cardiovascular patients with and without PAD,[15] a sample size of 24 per group was sufficient to detect a significant difference in HRV between groups (power $\geq$ 80%, $p < .05$).

Baseline characteristics

Demographic characteristics of the patients, including height, mass, body mass index (BMI), cardiovascular risk factors, comorbidities, and current medication were obtained from a medical history and physical examination at the beginning of the study. Obesity was defined as a BMI $>$30 kg/m^2. Hypertension was defined as a resting systolic blood pressure $\geq$140 mmHg or diastolic $\geq$90 mmHg on two or more occasions, or use of antihypertensive medications. Diabetes was defined as a fasting blood glucose $\geq$126 mg/dL or use of hypoglycemic medication. Coronary artery disease was defined as a history of myocardial infarction or surgical procedures, or use of anti-anginal medication.

Ankle/brachial index

Two experienced evaluators measured ankle and brachial systolic blood pressure simultaneously, as described and validated previously.[20] Brachial systolic blood pressure was measured by auscultation, and ankle (posterior tibial or dorsalis pedis) systolic blood pressure was assessed using a portable Doppler ultrasound unit (Medmega, DV 610, Ribeirão Preto, Brazil). Resting ABI was calculated for each leg (ankle systolic blood pressure divided by the greater of the left or right brachial systolic blood pressure) and the recording for the leg with the lowest ABI value was used for analysis.

Graded treadmill test

Patients performed a graded treadmill exercise test until limited by maximal claudication pain, as previously described by Gardner and Skinner.[21] Briefly, treadmill speed was maintained at 2.0 mph (3.2 km/h) with gradient increased 2% every 2 minutes. Maximal walking distance (MWD) was assessed as the distance at which the patient was unable to continue to exercise due to the sensation of pain, cramping, or burning that occurred in the calves, thighs, and/or buttocks.[22] Claudication distance (CD) was assessed as the distance the patient walked without pain. For analysis, patients were grouped into tertiles according to their MWD (i.e. low MWD, less than 290 meters; moderate MWD, between 291 and 533 meters; high MWD, more than 534 meters) and CD (i.e. low CD, less than 105 meters; moderate CD, between 106 and 220 meters; high CD, more than 221 meters).

Heart rate variability

For the determination of resting HRV, RR intervals obtained by a heart rate monitor (POLAR, RS 800CX, Lake Success, NY, USA) were recorded between 8:00 a.m. and 10:00 a.m. All patients were instructed to have only a light meal at least 2 hours before the recording and to abstain from smoking and drinking caffeine-containing beverages or alcohol for the previous 12 hours. They were also asked to avoid high intensity physical exercise for at least 12 hours before the recording session. Patients undertook a supine position for 20 minutes, with the final 10 minutes used to examine for resting HRV. All data were transferred and stored using Polar ProTrainer 5 software (Polar Electro, OY, Kempele, Finland). Two evaluators visually inspected the data and any inappropriate or premature RR interval was corrected by interpolating data. Any RR interval with a difference greater than 20% compared with adjacent intervals was